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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/912,818	07/24/2001	Daniel Pinkel	407E-914026US	8113

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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER
FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/912,818	PINKEL ET AL.	
	Examin r	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-86* is/are pending in the application.

4a) Of the above claim(s) *72,73 and 77-86* is/are withdrawn from consideration.

5)☒ Claim(s) *45-67* is/are allowed.

6)☒ Claim(s) *68-71 and 74-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 19, 2003, has been entered.

Status

Claims 45-86 are pending.

Claims 45-67 are allowed (in view of the terminal disclaimer).

Claims 68-71, 74-76 are rejected.

Claims 72, 73, 77-86 are withdrawn from consideration.

With regard to the restriction, it is noted that the 103 remains applicable for the reasons given in the advisory action. Specifically, the claims are not limited to "amplification" of the chromosomal segment at 17q22-q24 but are open to "gains". Even if the translocation is not treated as an "amplification", it is clearly a "gain" at that position, and the rejection is maintained. Therefore, the elected species is still rejected. This action is not final, however, because a new prior art rejection is made regarding the elected species.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Double Patenting

The rejection of claims 45, 46, 56 and 58-61 under the judicially created doctrine of obviousness-type double patenting is withdrawn in view of the terminal disclaimer.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 68, 69, 71 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Tsuda et al (Cancer Research (1989) 49:3104-3108).

Tsuda teaches method for detecting a copy number variation in a suspected breast cancer sample (see abstract) by detecting an amplification or gain of unique sequences (see abstract and page 3107, column 2, "Amplification of c-erbB2 was confirmed to be a factor indicating a poorer prognosis in breast carcinoma patients", also see figure 1, case A, where ear1 at position 17q21-22 is amplified) in at least one chromosomal region selected from the group consisting of:

on chromosome 17, about position q22 to about position q24 (see page 3104, column 2, "c-erbB-2 and one of the v-erbA-related genes, ear-1 are localized on chromosomes 17q21 and 17q21-22, respectively")

said method comprising:

(a) contacting a probe that binds selectively to a target polynucleotide sequence of said region with a nucleic acid sample prepared, directly or indirectly, from said

suspected breast cancer sample, wherein said nucleic acid sample comprises said target polynucleotide sequence and said probe is contacted with said sample under conditions in which said probe fonns a stable hybridization complex with said target nucleic acid sequence (see page 3105, column 1, subheadings "Patients" and "DNA extraction and slot-blot hybridization analysis", and figure 1); and

(b) detecting said hybridization complex (see page 3105, column 1, subheading "DNA extraction and slot-blot hybridization analysis" and figure 1).

With regard to claim 69, Tsuda teaches a labeled probe (see page 3105, figure 1, "hybridized to ^{32}P-labeled probe DNA").

With regard to claim 74, Tsuda teaches extraction of primary tumor cells, which inherently comprises genomic DNA (see page 3105, column 1, subheading "DNA extraction and slot-blot hybridization analysis").

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 68-71 and 74-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alitalo (Proc. Natl. Acad. Sci. (1983) 80:1707-1711) in view of Hainsworth et al (Cancer Genet. Cytogenet. (1991) 53(2):205-18).

Alitalo teaches a method for detecting an amplification of 8q24 comprising contacting a chromosome sample with a labeled nucleic acid probe which binds to 8q24, detecting the hybridization complex and determining the copy number of the sequence (page 1708, subheading "c-myc is amplified in COLO 320 genomes").

Hainsworth teaches that, at least in some instances, there is chromosomal gain at 17q23 in primary breast cancers (see table 2, case 907, where there is a derivative of chromosome 17 which is translocated in 17q23, which represents an gain at that position) .

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine amplification detection assays of Alitalo with the disclosures of specific regions of interest given by Hainsworth since an ordinary practitioner would have recognized that the extremely well known methods of southern blotting or in situ hybridization could be used to identify any specific desired chromosomal abnormality and an ordinary practitioner would have also recognized that the southern or in situ hybridization would have been useful as a diagnostic tool to

characterize known chromosomal abnormalities. Since Hainsworth suggests the association of the 17q23 region with breast cancer, an ordinary practitioner would have been motivated to use either southern hybridization or in situ hybridization to diagnose the presence or absence of a specific region in order to correlate the phenotypic syndrome with that region. Finally, an ordinary practitioner would have recognized that the nucleic acid sources are well known in the art as equivalents, so that either cDNA or genomic DNA are well known targets for analysis.

7. Claims 70, 75 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuda et al (Cancer Research (1989) 49:3104-3108) in view of Mullis et al (U.S. Patent 4,683,202).

Tsuda teaches the limitations of claims 68, 69, 71 and 74 as discussed above. Tsuda does not teach amplifying the DNA before detection or the use of cDNA.

Mullis teaches a polymerase chain reaction amplification method in which DNA is amplified prior to detection (see column 13, line 42 to column 14, line 17). Mullis further teaches the use of any DNA source, including cDNA (see column 5, lines 35-60). Mullis further teaches labeling of the sample DNA (see column 14, lines 8-17).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to amplify the sample of Tsuda as taught by Mullis since Mullis states

> "The method herein may also be used to enable detection and/or characterization of specific nucleic acid sequences associated with infectious diseases, genetic disorders or cellular disorders such as cancer. Amplification is useful when the amount of nucleic acid available for analysis is very small, as, for example, in the prenatal diagnosis of sickle cell anemia using DNA obtained from fetal cells.

> Amplification is particularly useful if such an analysis is to be done on a small sample using non-radioactive detection techniques which may be inherently insensitive, or where radioactive techniques are being employed but where rapid detection is desirable. (see column 13, lines 42-54)."

Thus, Mullis provides explicit motivation to amplify cancer related genes, such as the genes identified by Tsuda as associated with breast cancer, in order to perform rapid detection, which will minimize possible anxiety for breast cancer patients subject to the test, as well as more sensitive detection, to ensure that the cancer is detected even when the amount of material is very small. The practitioner in 1992 would have expected the PCR method of Mullis to function with a near absolute expectation of success.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JEFFREY FREDMAN
PRIMARY EXAMINER